REMARKS

Applicants have amended claim 1 to provide antecedent basis. Claims 1-26, of which claims 1, 13 and 14 are in independent form, are presented for examination.

Applicants have discovered methods of purifying substances, such as biological substances, from a mixture using magnetic particles that specifically bind to the substances. The methods include using a surface tension releasing agent to enhance adherence of the magnetic particles to a probe inserted into the mixture to remove the particles as completely as possible. None of the references cited by the Examiner discloses or suggest using a surface tension releasing agent to enhance adherence of the magnetic particles to a probe. Applicants believe that until the end of the 1990's, the only method used in practice in laboratories for separating magnetic particles was to draw them with an external magnet to a wall of a vessel and thereafter to remove the liquid from the vessel.

Under 35 U.S.C. § 103(a), claims 1, 2, 7-17, and 22-26 are rejected as being unpatentable over U.S. Patent No. 5,705,628 (Hawkins) in view of U.S. Patent No. 4,272,510 (Smith); and claims 1-6, 9, 13, 14, and 18-21 are rejected as being unpatentable over U.S. Patent No. 4,454,234 (Czerlinski) in view of Smith.

The Examiner has acknowledged that Hawkins and Czerlinski fail to teach using a magnetic probe to separate magnetic particles from a mixture and to transfer the particles, and has relied on Smith for the missing features. In combining Hawkins and Smith, the Examiner has reasoned:

> It would have been obvious to one of ordinary skills in the art to use the magnetic separation device of Smith et al. to separate bound magnetic particles in the method of Hawkins because Hawkins suggests magnetic separation step and transferring the magnetic particles to a second medium/vessel. By using the magnetic separation means of Smith, the magnetic separation step of Hawkins' method would be carried out at a faster pace thus would save much time and effort and the particles can be transferred to as many vessels as possible. Also, by using such combination, a large number of solid phases units (particles) can be separated simultaneously under extreme [sic, extremely] uniform conditions, so as to yield highly reproducible results in solid phase assays

> with large numbers of specimen. Regarding the concentration [of] the magnetic particles, it would have been obvious to one of ordinary skill in the art to adjust such concentration to execute optimum binding between the magnetic particles and the target analyte. (Office Action, page 3.)

This reasoning is flawed because the Examiner has misunderstood Applicants' invention. As indicated above, the use of a surface tension releasing agent enhances the adherence of the magnetic particles to a probe inserted into the mixture, not between the magnetic particles and the target analyte, as misunderstood by the Examiner.

The Examiner's reasoning is further flawed because it is not supported by the cited references. As acknowledged by the Examiner, Hawkins already discloses a magnetic separation techniques. Hawkins does not indicate any deficiencies with its technique. Thus, Applicants submit that one skilled in the art would not look elsewhere for another magnetic separation technique because Hawkins has already provided a suitable technique.

Nevertheless, the Examiner has suggested that the techniques of Smith allows the separation to be performed at a faster pace. Applicants believe the Examiner is referring to Smith's use of multiple receptacles simultaneously to support the position that Smith's technique is faster than Hawkins's technique. But of course there is no indication in Hawkins or Smith that one technique is faster than the other. Indeed, using multiple receptacles simultaneously is altogether distinct from Smith's use of magnetic probes; that is, it does not follow that one must use multiple vessels with Smith's magnetic probes. One can simultaneously use multiple receptacles without using magnetic probes. So, if one skilled in the art wants to quicken Hawkins's technique, one can also streamline Hawkins's technique simultaneously with multiple vessels, without using Smith's magnetic probes.

The Examiner has also suggested that Smith's technique would yield highly reproducible results because it is performed under uniform conditions. But it is Hawkins's technique that subjects the particles to the more uniform conditions. In Smith's technique, particles to be separated are placed in multiple receptacles; but in Hawkins's technique, the particles are placed in one vessel. Clearly, the particles in Hawkins's technique are subjected to the more uniform conditions since they are placed in the same environment.

Morover, one skilled in the art would also not use Smith's technique for the type of particles that Hawkins describes. Hawkins discloses using particles that range from about 0.1 micron mean diameter to about 100 microns mean diameter (col., 4, lines 12-14). Smith, on the other hand, discloses using much larger particles having a diameter range of from about 0.1 mm to about 2.0 cm (col. 3, lines 61-65). The relatively heavy macroscopic particles will tend to fall readily to the bottom, while microscopic particles move freely to form suspensions such that separation with a magnetic probe would be quite different. Also, the magnetic behavior of such macroscopic particles is very much different from that of a mass of microscopic particles. In light of these differences, one skilled in the art would further not be motivated to use Smith's techniques with Hawkins's system. For at least these reasons, claim 11, which recites that the size of the magnetic particles is less than 50 microns, should be allowed because one skilled in the art would not be motivated to use Smith's technique for particles less than 50 microns.

For at least these reasons, Applicants submit that the proposed motivation to combine Hawkins and Smith fails. Indeed, there is no motivation to combine the references as suggested by the Examiner.

Similarly, the motivation to combine Czerlinski with Smith is also flawed. Here, the Examiner has suggested:

> It would have been obvious to one of ordinary skills in the art to use the magnetic separation device of Smith for the magnetic separation step in Czerlinski's method because such as device would accelerate the collection of the magnetic particles and thus would accelerate the speed of the separation step so that results would be obtained at a faster rate since the method of Czerlinski requires that the magnetic particles must be collected and resuspended a total of three times. (Office Action, page 4, emphasis added.)

Here, Applicants submit that the Examiner has misinterpreted the cited references.

Nothing in Czerlinski suggests that its technique requires three suspensions. The Examiner has taken Czerlinski's examples, which Czerlinski has indicated as "illustrative" (col. 7, lines 27-29), to create motivation to combine the references. Furthermore, the Examiner has ignored that in all six embodiments that Smith describes, it states, "These and other combinations of manipulations can be repeated as required in the particular procedure being used." (See, e.g.,

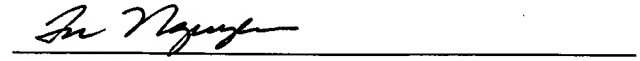
col. 5, lines 50-52; col. 6, lines 48-50; col. 7, lines 17-19; and col. 8, lines 6-8.) Thus, as with the Hawkins and Smith combination, nothing in Czerlinski or Smith indicates that one technique is faster than the other technique. Insofar as Smith describes using multiple vessels simultaneously, the technique of Czerlinski can also be adapted to be used simultaneously with multiple vessels and without using Smith's magnetic probe. The rejection, if maintained, would be based on improper hindsight reasoning.

Applicants submit that the proposed motivation to combine the references is not supported by the references. None of the references cited by the Examiner discloses or suggest using a surface tension releasing agent to enhance adherence of the magnetic particles to a probe. If the combinations suggested by the Examiner were reasonable, Applicants submit that such combinations would have been commercially available. As such, it appears that those skilled in the art do not consider Smith's technology useful and have not tried to combine it with the technologies of Hawkins or Czerlinski. In light of the above remarks, Applicants request that the rejections be reconsidered and withdrawn.

Enclosed is a Petition for Extension of Time with the required fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: May 4, 2004



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